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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/602,800	06/23/2000	David B. Agus	P1760R1	1759

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EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/602,800	AGUS ET AL.	
	Examiner	Art Unit	
	Anne Holleran	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 22-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 22-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/20/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 3/24/2004 is acknowledged. Claims 1, 2, 5, 22, 23, 28, 30 and 31 were amended.

2. Claims 1-9 and 22-31 are pending and examined on the merits.

Claim Rejections Withdrawn:

3. The rejection of claims 1-9 and 22-28, 30 and 31 under 35 U.S.C. 102(e) as being anticipated by Ross I (U.S Pre-Grant Publication 2002/0076695; published June 20, 2002; effective filing Sep. 14, 1998) as evidenced by Reese (Reese, D. et al. Proceedings of the American Association for Cancer Research, 37: page 51, March 1996; Abstract #353) is withdrawn in view of the amendment to claims 1, 22 and 31.

4. The provisional rejection of claims 1-9 and 22-31 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 28-40, and 42-62 of copending Application No. 08/948,149 is withdrawn in view of an amendment in copending application No. 08/948,149 deleting the use of monoclonal antibody 7F3 from the claimed methods.

5. The provisional rejection of claims 1-9 and 22-31 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 42, 45, 55 and 66 of

copending Application No. 09/705,579 is withdrawn because claims 55 and 66 have been canceled and because the claims do not currently recite the use of monoclonal antibody 7F3.

Claim Rejections Maintained:

6. The rejection of claims 5, and 23 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection over claims 5 and 23 is maintained because these claims contain the recitation "monoclonal antibody 2C4 (ATCC HB12679) or a humanized form thereof". The specification defines humanized 2C4 antibody as an antibody "possessing antigen binding amino acid residues of murine monoclonal antibody 2C4". This definition fails to limit the scope of humanized 2C4 antibodies to those antibodies that bind to the same epitope as that of monoclonal antibody 2C4 (ATCC HB12679) and fails to provide adequate structural description of the antibody. The phrase "possessing antigen binding amino acid residues of murine monoclonal antibody 2C4" may mean that a "humanized 2C4 antibody only possesses a one or two of the CDR residues of murine monoclonal antibody 2C4. Without a recitation in claims of the epitope to which the humanized antibody binds or a definition in the claims clearly stating the binding specificity of the humanized antibody, or a definition in the specification clearly setting forth the structure of humanized 2C4 antibodies, the phrase "monoclonal antibody 2C4 (ATCC HB12679) *or a humanized form thereof*" reads on a genus of antibodies defined only by function (i.e. binds ErbB2 and blocks ligand activation of an ErbB receptor), for which

the descriptioin of 2C4 is not representative. Therefore, the specification lacks an adequate written description of a humanized form of monoclonal antibody 2C4(ATCC HB12697) and an adequate written description of the claimed methods of using such antibodies.

7. The rejection of claims 1-9 and 22-31 under 35 U.S.C. 103(a) as being unpatentable over Hudziak (U.S. Patent 5,725,856; issued 03/1998; effective filing date 01/1988) and Ross II (U.S. Patent 5,994,071; issued 11/1999; filing 04/1997); in view of Sliwkowsky (Sliwkowsky, M.X. et al, J. Biol. Chem. 269: 14661-14665, 1994) or Klapper (Klapper, L.N. et al. Oncogene, 14: 2099-2109, 1997); and further in view of Plowman (U.S. Patent 5,804,396; issued 09/1998; effective filing 10/1994) or Akita (U.S. Patent 5,968,511; issued 10/1999; effective filing 03/1996) or Greene (U.S. Patent 6,417,168; issued 07/2002; effective filing 03/1998) is maintained for the reasons of record.

Applicants argue that the prior art of record fails to make obvious the claimed methods of treating prostate cancer with an antibody that binds ErbB2 and blocks ligand activation of an ErbB receptor substantially more effectively than humanized monoclonal antibody huMab4D4-8 (Herceptin®). This argument is not found persuasive because fhe fact that monoclonal antibody 2C4 is more effective than huMab4D5-8 in blocking ligand activation of an ErbB receptor is not the only motivation for using 2C4 in the claimed methods. Sliwkowsky teaches a specific monoclonal antibody 2C4 and teaches that it was antibody that inhibits the activation of ErbB2 by heregulin. Because the prior art recognized that prevention of ErbB2 oligomerization induced by ligands such as heregulin was a therapeutic target for the treatment of cancer, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to

have used the monoclonal antibody 2C4 of Sliwkowsky because Sliwkowsky teaches that monoclonal antibody has this function. Furthermore, the monoclonal antibodies of Klapper would also have been useful for the purpose of treating prostate cancer through the inhibition of heregulin activation of ErbB receptors.

The claimed inventions are drawn to methods for the treatment of prostate cancer comprising the administration of antibodies that inhibit ligand activation of an ErbB receptor substantially more effectively than humanized monoclonal antibody huMab4D5-8 (Herceptin). Hudziak teaches methods of inhibiting the growth of tumor cells by administering to a patient antibodies capable of inhibiting Her2 (ErbB2) function, and teaches methods of inhibiting the growth of tumor cells that overexpress a growth factor receptor (see col. 4, lines3-31). Hudziak fails to appreciate that prostate cancer cells would be a target. Ross II teaches prostate cancer cells over express ErbB2 (see col. 6, lines 25 – 51), and that expression of ErbB2 is associated with poor prognosis in prostate cancer. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used anti ErbB2 antibodies that inhibited the function of ErbB2 for the treatment of prostate cancer.

While the combination of Huziak and Ross II teaches generally methods for the treatment of prostate cancer comprising the use of antibodies that bind to ErbB2, and Hudziak contemplates antibodies that bind to ErbB2 and inhibit ligand binding to an ErbB growth factor receptor, or the down regulation of the growth factor (see col.5, lines 38-64), the combination of Hudziak and Ross fail to specifically teach methods comprising the use of antibodies that inhibit the formation of an ErbB hetero-oligomer. However, such antibodies are known in the art, as evidenced by the teachings of Sliwkowsky that monoclonal antibody 2C4 inhibits the activation

of ErbB2 by heregulin (see page 14663, 1st col.). Also, Klapper teaches antibodies that bind to ErbB2 and inhibit interaction of ErbB2 with other ErbB receptors (see pages 2102 –2105). Additionally, the prior art, as evidenced by Plowman, Akita and Greene, recognizes that the inhibition of ErbB2 oligomerization with other ErbB receptors is a therapeutic target for the treatment of cancer. Plowman teaches thereapeutic agents that inhibit signal transduction by Her-2 heterodimers (see abstract and col. 4, lines 31-49). Akita teaches antibodies that bind to ErbB3 that inhibit the binding of heregulin-induced formation of an ErbB2-ErbB3 heteroligomer, and teaches the use of such antibodies in the treatment of cancer (prostate cancer is contemplated), in which excessive activation of the ErbB2-ErbB3 complex is occurring (see abstract, and col. 29, lines 9 – 23). Greene teaches methods for treatment of cancer comprising administering a peptide that inhibits the formation of ErbB protein dimers, where the dimers may be heterodimers (see claims 1 and 14; and col. 9, lines 15-21).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the antibodies of either Sliwkowsky or Klapper in the method of Hudziak for the treatment of prostate cancer. One would have been motivated to use antibodies that inhibited ligand activation of an ErbB receptor in view of the fact that the art recognized that ErbB2 was activated by the formation of heterodimers and that ErbB2 activation plays a role in the growth of prostate cancer cells.

8. The provisional rejection of claims 1-9 and 22-31 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4-9, 16-22, 24-27, and 60-63 of copending Application No. 09/602, 812 is maintained for the reasons of record.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of Application No. 09/602,812 are drawn to methods for treating cancer with an antibody that inhibits ligand activation of an ErbB receptor. A preferred embodiment described in the specification is prostate cancer.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant argues that only the claims of applications may be compared in order to make a double-patenting rejection, and that the reliance on the teachings of the specification that a preferred embodiment in one application is the same as the claimed invention of a second application is improper. Applicant also states that a restriction requirement was made in copending application 09/602,812. With regard to the restriction requirement in 09/602,812, the requirement was an election of species requirement for the purposes of focusing the initial search of the prior art. Upon allowance of any generic claim, a species reading of the claim will be allowable. Furthermore, it is proper to use the specification to determine preferred embodiments of generic claims for the purposes of making a double-patenting rejection. Therefore, the provision double-patenting rejection is maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (571) 272-0841.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 571-1600.

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Anne L. Holleran
Patent Examiner
June 14, 2004